Division of Microbiology and Infectious Diseases
SAE Recording and Reporting Guidelines for Single Study Product
SAE HOTLINE 1-800-201-8725
SAE FAX 1-888-488-9697 or 910-772-7069

Make copies of the blank SAE report form as needed. Retain originals with confirmation of all information faxed to PPD Development.

All serious adverse events (SAEs) must be **reported within** one business day of site awareness to the Medical Affairs/Pharmacovigilance Department at PPD Development by telephone or facsimile of the completed SAE report form.

**If there is any question as to whether an event should be reported or how to complete the SAE form, call PPD.**
**SAE HOTLINE 1-800-201-8725**

## GENERAL INFORMATION

### Adverse Event (AE) Definition (ICH GUIDELINES E6 FOR GCP 1.2):

Any untoward medical occurrence in a patient or clinical investigation subject administered a pharmaceutical product and which does not necessarily have a causal relationship with this treatment. An AE can therefore be any unfavorable and unintended sign (including abnormal laboratory finding), symptom or disease temporally associated with the use of a medicinal (investigational) product, whether or not related to the medicinal (investigational) product.

### Serious Adverse Event (SAE) Definition (21 CFR CH.1 PART 312.32):

Any adverse drug experience occurring at any dose that results in any of the following outcomes:

- Death
- Immediately life threatening
- Persistent or significant disability/incapacity
- Inpatient hospitalization or prolongation of existing hospitalization
- Results in a congenital anomaly/birth defect
- Important medical events that may not result in death, be life threatening, or require hospitalization may be considered a serious adverse drug experience when, based upon appropriate medical judgment, they may jeopardize the patient or subject and may require medical or surgical intervention to prevent one of the outcomes listed in this definition.

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## GENERAL INSTRUCTIONS

1. Elective procedures requiring hospitalization will not be considered SAE's if they were pre-planned prior to signing consent; however, other events may occur during this hospitalization that may be considered serious or non-serious adverse events and will need to be captured according to the protocol.

2. Terms such as **death, hospitalization or a procedural name are not acceptable event terms.**
   - Example: Subject was hospitalized for cholecystectomy due to cholecystitis. The event term would be "Cholecystitis" (not the procedure).
   - Example: "Death" is an outcome not an event term. The investigator should report the primary cause of death as the SAE term.

3. All initial SAE reports must have the relationship to study medication documented. If an expedited report is required, PPD will contact the site for further medical information regarding the event. The information will need to be provided to PPD as quickly as possible.

4. All SAEs will be:
   - Followed to resolution (subject's health has returned to his/her baseline status or all variables have returned to normal) or
   - Followed until stabilization of the event has occurred (the investigator does not expect any further improvement or worsening of the event) or
   - The event is otherwise explained regardless of whether the subject is still participating in the study.
   - Some events do not end, such as metastasis; however, once these events are determined by the principal investigator to be stable or chronic, the PI may consider the event to be resolved or resolved with sequelae.

5. In case of death:
   - The SAE should be the cause of death (do not use the term "death" and avoid using cardiac arrest or respiratory failure if possible. Instead provide the diagnosis leading to cardiac arrest or respiratory failure.)
   - There should be only one SAE with an outcome of death for each subject.
   - For other adverse events that were ongoing at the time of death, enter outcome of these events as 'Ongoing'.
   - The severity should be Death or Grade 5 if a toxicity table is provided.
   - Please submit a copy of the Death Summary and Autopsy Report (if applicable).

6. **PROTECT YOUR SUBJECT'S IDENTITY:**
   - Obliterate the subject's name in the header as well as in the body of the text on any supporting documents. Replace it with the subject's number **(no initials)** prior to faxing/mailing any data.
   - The individual who obliterates the subject's identity must date and initial the obliteration.
   - Obliterate the medical record number, account number, social security number, date of birth and any parent or spouse information such as names and address.

7. Review all source documents (examples - hospital discharge summary, hospital notes) as additional SAEs may be detected. If there are any questions as to whether you think an additional SAE may be present, please call PPD to discuss. [i.e. Subject was hospitalized for pneumonia (one SAE). Subsequently, the subject falls out of bed and fractures the left femur and requires extensive surgery 3 days after the initial admission. Fractured left femur could be a second SAE if assessed by the investigator as serious because the subject had to go to surgery. Ten days after the initial admission, the subject still has pneumonia. On day 10 after admission, the subject experiences myocardial infarction, which results in death. Myocardial infarction would be a third SAE and would have an outcome of death. The pneumonia and the fractured left femur would be considered ongoing.]

8. **FOLLOW-UP SAE FORM COMPLETION INSTRUCTIONS**:
   - Before any changes are made on the original SAE form faxed to PPD, make a copy of the SAE forms.
   - On the copy, make any changes, additions or updates. All changes should be neat and legible.
   - Initial and date all changes only.
   - At the top of the first page indicate the follow-up number the form represents and fax in all three pages even if changes were only made to one or two of the pages.
   - Fax to PPD PVG
   - Retain all fax confirmations with the items faxed.
   - For subsequent changes or additional information to the SAE form, always take the last SAE follow-up form sent to PPD, make a copy and then make all changes on the COPY. Fax this copy and again retain fax confirmation for site records. Repeat the process for all subsequent follow-ups.

9. **DOWNGRADING/DELETION OF A PREVIOUSLY REPORTED SAE**: If the PI determines a previously reported SAE doesn't meet serious criteria, follow the steps below to delete/downgrade the SAE:
   - Complete a Follow up SAE report as above.
   - Document in the "Event Summary" section a brief explanation of why the PI determined the event to not be serious (i.e., "it was determined that the subject was not hospitalized; therefore, this event does not meet serious criteria" or "the event was determined to be past medical history.")

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## SAE FORM COMPLETION INSTRUCTIONS

- All date formats should be written as a two-digit date, three-**letter** month abbreviation and four-digit year (i.e. DD/MMM/YYYY).
- If your study is not obtaining certain information requested, complete the field with N/A (not applicable).

### Page 1 of the SAE Report Form : ONE EVENT PER FORM

1. **Complete:**
   - "Site name/number" (if you do not have a number just include the name of the PI), "center number" if applicable and "subject number"
   - Provide the date the site first became aware of the event
   - If the report has never been submitted complete the "Initial report date." For follow-up reports complete the "follow-up report date" and the number in consecutive order (i.e., Follow-up # 1 or Follow-up #2).
   - **Section 1.**
     - "Age at onset of SAE" **– do not provide date of birth.**
     - "Gender" – check male or female
     - "Weight" – enter number and mark lbs., kgs., or gms.

2. **Section 2. "SAE Category":**
   - Check all appropriate categories indicating an SAE
   - If the event prolonged hospitalization, mark the box "hospitalization/prolonged hospitalization" and circle "prolonged hospitalization"
   - If other is chosen, specify what this is.

3. **Section 3-6. "Study Product Information":**
   - Complete the study product name. If study product is blinded, indicate as such.
   - Include dose, route and schedule of study product at SAE onset (for example indicate if the event occurred after the third dose in a series of four).
   - Provide the date treatment/therapy with study product began.
   - Provide the last date study product was taken prior to the onset of this SAE.

4. **Section 7. "Event":**
   - Provide the event term using a medical diagnosis or the cause of death. There should only be one term or diagnosis for each report. Do not indicate all the symptoms as the event term. For example, use dehydration and not nausea, vomiting and diarrhea.

5. **Section 8. "Onset Date":**
   - The date the investigator considers the event to meet one of the serious categories will be the start date of the event.

6. **Section 9. "Severity"** (check in only one column and only one item in that column)**:**
   - **Mild** - causes minimal discomfort and does not interfere with normal activities.
   - **Moderate** - sufficiently discomforting to interfere with normal activities.
   - **Severe** - incapacitating, prevents normal activities.
   - **Life-Threatening –** immediately life threatening however death did not occur.
   - **Death**
   - **Or** if a toxicity table is included in the protocol, use the grading scale provided **Grade 1 – Grade 5 – see toxicity table**.

7. **Section 10&11. "Relationship":**
   - Provide the investigator's assessment of the relationship between the study product and this SAE. **This must be answered**.
   - If not associated is indicated, then choose the cause for this SAE.
   - **Indicate in the event summary if event is associated with concurrent illness/condition, concomitant medication or anything else**.

8. **Section 12. "Study Procedure Status":**
   - Indicate the action taken with the study product because of this SAE.
   - Do not mark permanently discontinued if the event is due to a death.
   - If the study product is only given one time for the entire study, then mark "not applicable for one time dose."

9. **Section 13. "Outcome" (choose one):**
   - For "resolved without sequelae," provide "date of resolution."
   - For "resolved with sequelae," provide "resolution date" and indicate the sequelae (a condition following a consequence of a disease, example: if the event is "Stroke" the sequelae may be "numbness in right/left arm and leg").
   - If death is chosen:
     - Include date of death
     - Provide the autopsy report if one will be done.
     - The "outcome" for the event that caused the death should be entered as "DEATH" on the SAE report. Only ONE event per subject will have an "outcome" of death.
     - For SAEs that did not cause the death and were not resolved prior to the death, the outcomes for these events will be entered as "Ongoing."
   - "Stop date" of the event should be the date the event is no longer present or stabilizes. If there are lingering effects after a subject is discharged then the event will not resolve until all symptoms have ceased or stabilized. If the "outcome" is

"resolved with sequelae" (a condition following the consequence of a disease) the sequelae must be listed (i.e. if the SAE is "Stroke" the sequelae may be "numbness in right arm/left arm and leg").

**PAGE 2 of the SAE Report Form**

1. **Complete:**
   - "Site name/number" (if you do not have a number just include the name of the PI), "center number" if applicable and "subject number"

2. **Section 14 and 15. "Relevant Lab and Diagnostic Tests":**
   - List any abnormal laboratory or diagnostic tests relevant to this adverse event. **Do not include information not pertinent to this event.**
   - Include information regarding previous labs or tests prior to this event onset.
   - Copies of all relevant lab or diagnostic tests/reports should be submitted with the SAE report. Write "see attached" in this area of the report when faxing source documents.
   - If no tests were performed mark "no relevant tests."
   - If results are pending, mark "pending" and specify pending tests.

3. **Section 16. "Concomitant Medications":**
   - Provide all relevant medications the subject was taking up to one month prior to the onset date of the SAE.
   - Include the total daily dose and the start and stop dates as well as the indication.
   - Also, mark "yes" if the investigator suspects the concomitant medication to be the cause of the SAE.
   - If there are no relevant medications, then mark "no relevant concomitant medications."

**PAGE 3 of the SAE Report Form**

1. **Complete:**
   - "Site name/number" (if you do not have a number just include the name of the PI), "center number" if applicable and "subject number"

2. **Section 17. "Event Summary":** Complete the event summary to include at a minimum the information in the format below. Add additional pages if needed. A typed summary is acceptable and should be signed, dated and submitted with the SAE forms.
   **Example**:

This [age at time of enrollment or at time of event] [week/month/year] old [race and gender] with [indication if appropriate] began trial therapy [details of drug administration, dose, etc. as appropriate] on [date].

On [date] the subject experienced [event as reported]. Include setting of the event, details of severity, duration, treatment for the event, relevant laboratory, radiology or other diagnostic results.

Relate event to appropriate medical history. [Cigarette, alcohol, personal family history, relevant allergies to meds, relevant personal/social history or previous relevant diagnoses.]

The study product was [increased, reduced, unchanged, permanently discontinued, temporarily withheld or not applicable for one time dose] due to this event. The subject [outcome: recovered on {date}, recovered on {date} with sequelae, died on {date}, or continued to experience {event term}] at the end of the study.

The investigator considered the event [was, was not] associated to the study drug administration because [consistent with animal findings, concomitant med, concurrent disorder, other.] Pending information [follow-up diagnostic testing, discharge date, autopsy findings, etc.]

3. **Signatures:**
   - **"Person completing this form":** provide the printed name, signature and date of the individual completing the SAE form.
   - **"Investigator's Name":** provide the investigator's printed name, signature and date for each report.
     - Do not hold the submission of an SAE if the PI is not available to sign the initial report. The study coordinator and sub-investigator should sign the SAE report if the PI is not available.
     - Any changes must be documented on a SAE form checked as follow-up. Indicate follow-up number in sequential order of submission.
     - **FAX SAE reports to PPD/PVG to 1-888-488-9697 or 1-910-772-7069**
   - It is MANDATORY that the Principal Investigator (PI) or sub-investigator on the FDA 1572, sign the SAE report if the event is downgraded to an adverse event or deleted as an adverse event.
   - Provide dates the initial and follow-up SAE forms were submitted, mailed or faxed to the required areas.